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Review Article

The use of photodynamic therapy in the treatment of cutaneous warts - a review

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ABSTRACT

Cutaneous warts are benign skin lesions caused by human papillomavirus infection and represent a common dermatological condition. Although often asymptomatic, warts may cause physical and psychological discomfort, particularly when persistent, painful, or located in visible areas. Conventional treatment methods show variable efficacy, recurrence and adverse effects. Photodynamic therapy has emerged as a minimally invasive therapeutic alternative with promising outcomes. The objective of this study is to evaluate the efficacy and safety of photodynamic in the treatment of cutaneous warts through an analysis of scientific literature, using databases. Articles published in English between 2020 and 2025 were analyzed using keywords: "warts," "verruca," "human papillomavirus," and "photodynamic therapy." The findings suggest that photodynamic therapy is a valuable therapeutic option for cutaneous warts, particularly resistant to conventional treatments, offering selective tissue destruction and minimal invasiveness. However, further large-scale randomized trials could help standardize protocols and confirm its comparative effectiveness.

Key words: Warts, Verruca, Photodynamic therapy, Therapy, Photodynamic, Photochemotherapy

INTRODUCTION

Warts or verrucae are manifestations of diseases caused by human papillomaviruses (HPV), which are commonly associated with cancers like cervical, anal and oropharyngeal cancers [1,2]. Various identified HPV genotypes can be classified into several clinical groups associated with genomic sequences. Following the aforementioned categorization, infections can be divided into non-genital cutaneous disease, anogenital disease, non-genital mucosal disease, and the rare but characteristic condition, known as epidermodysplasia verruciformis. What is particularly noteworthy is that the cutaneous infections are associated with at least 15 genotypes of HPV [3], and they clinically manifest as flat warts (verruca plana, on hands and face), common warts (verruca vulgaris), plantar warts (verruca plantaris, on soles of feet) [4]. Depending on their specific subtype and anatomical localization, warts may take on a variety of morphological forms like papillomatous structures, hemorrhagic points and lines surrounded by a whitish halo (Frogspawn pattern), yellowish structureless with bleeding streaks and spots or even interrupted skin lines and brown colored background [5,6]. Risk factors of cutaneous warts incluce using communal showers, occupational handling of meat and immunosuppression – for example among people who used a communal shower, the prevalence of warts on the feet reaches 27% [7]. Despite their often benign and asymptomatic nature, cutaneous warts are a common medical condition—whose prevalence in the general population is estimated

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at 7–12%—may become a source of psychological and physical discomfort [5,8], particularly when located in visible areas or when painful. Consequently, even though they may not present any clinical signs, the therapy of cutaneous warts is still required. There are different approaches for treatment of cutaneous verrucas. One of the most popular ways is to exfoliate the epidermis with for example, salicylic or lactic acids. Apart from that, cryotherapy, laser therapy (e.g.: CO2 laser, PDL, or YAG laser), 5% imiquimod cream or even injections of bleomycin or Candida albicans antigen are used [8,9]. Each of these treatments has specific advantages and limitations and therapeutic success often depends on factors such as the patient's immune status, wart subtype, duration of lesions and prior treatments. Among various interesting procedures, one of the techniques remains promising. The medical strategy known as photodynamic therapy is used not only for wart treatment, but also for treating acne vulgaris [10,11], various precancerous states of the vulva [12], psoriasis [11], atopic dermatitis, vitiligo [13], or even wound healing [11]. What is more, it is said to demonstrate the potential for high effectiveness [14]. The technique involves the application of a photosensitizer, a light-sensitive compound that accumulates in pathological tissues. One of them, for instance, is 5-Aminolevulinic acid (ALA) - commonly used to treat squamous cell carcinoma and prostate cancer, or Methylamine levulinate hydrochloride (MAL) - for basal cell skin cancer treatment [15]. The affected area is then irradiated with light of an appropriate wavelength and intensity, leading to the selective destruction of diseased cells [11,16]. PDT has therefore gained significant attention as a potentially effective, minimally invasive, and cosmetically favorable method for managing treatment-resistant or recurrent warts. The aim of this article is to determine whether photodynamic therapy can be considered an effective therapeutic intervention against various types of cutaneous warts, including flat warts, common warts, and plantar warts, and to assess its potential advantages over conventional treatment methods.

MATERIALS AND METHODS

Scientific articles addressing the use of photodynamic therapy in the treatment of warts were identified through an analysis of databases such as PubMed and Scopus using keywords such as "wart", "verruca", "human papillomavirus", "photodynamic therapy". Researchers included scientific studies published in English between 2020 and 2025.

Ethics Statement

Not applicable.

RESULTS

The results of the analysis are presented in Table 1. The analyzed studies demonstrated that photodynamic therapy is an effective treatment for various types of cutaneous warts, including verruca plana, verruca vulgaris, and verruca plantaris. Reported clearance and cure rates ranged from approximately 40% to over 85%, with several studies documenting excellent clinical responses and occasional complete remission without recurrence. Photodynamic therapy showed superior outcomes compared with intense pulsed light alone or topical photosensitizer application without illumination.

Considerable heterogeneity in treatment protocols was observed across studies.

DISCUSSION

Efficacy: The efficacy of photodynamic therapy can be assessed using articles highlighted in Table 1. Nearly all studies showed that PDT is an effective treatment method for cutaneous warts. The disappearance of warts fluctuates between 46.1% [17] and 52.4% [18], while the cure rate ranges between 40.9% [19] and 86.36% [20] with reports of complete clearance and no recurrences [21]. Meanwhile, the majority of response rates oscillate around an excellent response: 52.9% for daylight treatment and 29.4% for pro-yellow laser treatment [22]; 46.67% for complete response and 40.0% for excellent response [23]; 73.7% for red light therapy and 66.7% for daylight therapy [19]. Consequently, the studies provide mainly positive findings on the effectiveness of PDT therapy for the treatment of cutaneous warts.

Comparison of photodynamic therapy and alternative medical techniques: The following comparison of the method described in the title with other medical techniques – intense pulsed light [18,19] and injections of candida albicans antigen [17] or vitamin D3 [20] – shows that the results appear noteworthy. With intense pulsed light, the polychromatic, broad-spectrum light is

Table 1: Studies analyzed and organized with names of the authors, publishing date and country, the type of study, sample size and patient characteristics, wart type, methods (example: treatment protocols), results (example: clinical efficacy)

Authors, Date, Country	Type of study	Sample size and characteristics	Type of warts	Methods	Results
Hassan G. F. R., et al., 2025, Egypt	Original research article	42 patients with at least four cutaneous warts	Verruca plantaris, verruca plana, verruca vulgaris	Division of skin lesions for each patients: Group (1) - topical 10% liquid crystal loaded methylene blue, then was subjected to two passes of IPL with a 650 nm cutoff filter; Group (2) - to two passes of IPL; Group (3) - topical 10% liquid crystal loaded MB gel. They underwent four sessions at 2-week intervals. Control group (4) - no treatment	Disappearance of warts: Group 1 – 52.4%, Group 2 – 19%, Group 3 – 4.8% Best outcomes – verruca plantaris, then verruca plana and verruca vulgaris.
A Nassar, et al., 2020, Egypt	Comparative controlled study	39 patients of both sexes who had not undergone any treatment for past 3 months	Verruca plana	Group I – photodynamic therapy with methylene blue followed by IPL illumination. Topical methylene blue 10% solution applied for 60 minutes. Then IPL illumination parameters: single pass of IPL (hair mode), cut-off filter: 640 nm (the peaks of absorption of methylene blue: 610 and 660 nm), IPL settings: fluence (13-16 J/cm2); pulse duration of 20ms; 20ms pulse delay. The procedure repeated every two weeks until full remission or up to a maximum of three sessions, Group II – immunotherapy with 0.1 ml of candida albicans antigen (Injection with 0.1 ml of 1/100 solution of candida albicans antigen into the largest wart using a 100-unit insulin syringe. The procedure repeated every two weeks until full remission or up to a maximum of five sessions.), Control Group III – 0.1 ml saline. (Injection with 0.1 ml of saline into the largest wart using a 100-unit insulin syringe. The procedure repeated every two weeks until full remission or up to a maximum of five sessions.)	Disappearance of warts: Group I – 46,1%; Group II – 61,5%; Group III – no response. Side effects comparable in groups I and II.
Elshabory O., et al., 2025, Egypt	Prospective comparative clinical study	34 patients with one or more common warts (≥ 1 warts) and no history of previous treatment	Verruca vulgaris	Division into equal groups. Group I – for normal skin, the chemical sun block was used for thirty minutes before applying gel with 10% methylene blue on a wart. After that patient stayed outdoors exposing lesions at day light for 15 minutes. Procedure repeated every week until clearance or until 4 weeks. Group II – 5% lidocaine cream was applied 30 minutes before using 10% methylene blue on a wart. After 15 minutes patients were treated with 577-nm pro-yellow laser (Quad- roStar PRO YELLOW Asclepion Laser Technologies, Germany) with a fluence of 18 J/cm2 in the basic mode of the device.	The response rate: excellent: 75–100% reduction in wart size (in mm), very good: 50–75%, good: 5–50%, poor 0–25%. Group I: Excellent response 52.9%, very good 23.5%, poor 11.8% Group II: Excellent response 29.4%, poor 29.4%, no response 41.2%
Li Pomi F., et al., 2025, Italy	Case report	25-year-old man with multiple papules on a long-standing tatoo on right forearm	Verruca plana	Treatment: three sessions of conventional PDT at monthly intervals using a 10% ALA ointment (Biosynth AG, Staad, Switzerland) under occlusion. After three hours – irradiation was applied with diode red light at 630 nm in wavelength (S630, Alpha Strumenti, Milan, Italy). Position of light source: 50 mm from the skin surface (160 mW/cm2). Time: 8 min. Total light dose of 75 J/cm2. The procedure was well tolerated by the patient, who complained of just a mild burning sensation during the light exposure.	Three-month follow-up: complete clearance of the warts with no recurrences or modification of the tattoo's appearance. One-year follow-up: no recurrences or onset of new lesions.
Zhang W., et al., 2023, China	Retrospective study	15 patients (7 patients – progressive disease and 8 – stable disease) The number of warts in each location were documented as follows: right cheek (784), forehead (630), left cheek	Verruca plana on face	Application of 10% aminolevulinic acid (Shanghai Fudan Zhangjiang Biomedical Co., Ltd., Shanghai, China) in 0.9% saline, covering with plastic film and light shield were followed by, exposing the lesions to 635 nm red light for 20 min at an illumination distance of 11±1 cm and an energy density of 50–60 J/cm2 (LED-IB PDT instrument, Yage Optic and Electronic Technique Co. Ltd., Wuhan, China). Treatment repeated once	The response rate: complete response: 100%, excellent: 70-100%, good: 30-70%, poor: < 30%. 46.67% - complete response, 40.00% - excellent, 6.67% - good,

(Contd...)

Table 1: *(Continued)*

Authors, Date, Country	Type of study	Sample size and characteristics	Type of warts	Methods	Results
		(575), mandible (213), nose (97). 10 received three treatment sessions, 5 received two sessions.		every two weeks for a total of two or three sessions.	6.67% - poor; total effectiveness – 86.67%
Ibrahim NA., et al.,2020, Egypt	Randomized comparative controlled study	56 patients with resistant palmoplanter warts	Verruca plantaris	Random division into three groups. Group A (Intralesional Vit-D3 injection) After using topical anesthesia under occlusion, 18 patients were injected intradermally 0.2 mL of Vit-D3 amp (Devit-3 amp, 300,000 I.U/1 mL, manufactured by DEVA, Turkey). Treatment repeated monthly for maximum of 4 sessions. Group B (Photodynamic therapy): After applying Eosin-Trans as a photosensitizer fo 30 minutes, lesions of 22 patients were exposed to LED of wavelength 520 nm for 15 min with light dose of 34 J/cm2. Treatment was repeated every 2 weeks for maximum 8 sessions. Group C (Control): 16 patients were using topical Collomak manufactured by October pharma SAE.	Group A: Cure rate – 88.89%, Average treatment duration – 14.44±5.68 weeks, Number of sessions – median 3 sessions. Group B: Cure rate – 86.36%, Average treatment duration – 12.46±4.18, Number of sessions – median 6 sessions, Complete 100% response in 6 patients with subungual warts. Control Group: Cure rate – 18.75%
Li Pomi F., et al., 2024, Italy	Randomized double-blind trial	68 patients: group A – 38 patients (22 males, 16 females); group B – 30 patients (16 males, 14 females)	Verrucae vulgaris on hands	Random division into two groups. Group A: After applying 10% ALA (Biosynth AG, Staad, Switzerland) in polyethylene glycol ointment and 3 hours occlusion, the irradtiation with diode red light at 630 nm (S630, AlphaStrumenti, Milan, Italy) was added. Position of light source: 50 mm from the skin surface (60 mW/cm2). Duration: 8 minutes. Total light dose: 75 J/cm2. Group B: Following 15 minutes of using a sunscreen with SPF of 30, the 10% aminolevulinic acid in polyethylene glycol ointment was applied for 30 minutes, uncovered. Patients stayed continuously exposed to daylight after the procedure for 2 hours. Both techniques were repeated 3 times at 1 month-intervals.	Rate response: excellent (75–100% reduction of total wart count), partial (74–25%), and none (< 25% reduction or no response). Clinical follow-up after 1 year (W52) was also performed. Group A: excellent response – 73.7%, partial – 5.3%, none – 21.1%, relapses – 31.6%. Group B: excellent response – 66.7%, partial – 13.3%, none – 20.0%, relapses -26.7%
Hassan SNE., 2021, Egypt	This prospective randomized controlled trial	80 patients diagnosed verrucae were included in this study		Ramdom division into 3 groups. Group A (30 patients) received MB/IPL/PDT sessions. Group B (30 Patients) received IPL sessions. Group C (control).	Group A: Cure rate – 40.9%, ImageJ analysis – 80.05±27.12% reduction of verrucae and 89.28±19.19% for vessels and haemorrhagic dots, Clinical and dermoscopic clearance – 43.3%. Group B: Cure rate – 23.4%, ImageJ analysis – 48.16±34.21% reduction of verrucae and 65.99±30.58% for vessels and haemorrhagic dots, Clinical and dermoscopic clearance – 20%

PDT -photodynamic therapy; IPL - Intense pulsed light; MB – methylene blue; ALA – 5-Aminolevulinic acid; LED - light emitting diode

emitted. What is more, apart from a flashlamp, filters that prevent the delivery of light with wavelengths shorter than required can be used. IPL, serves as a medical strategy for telangiectasias, hyperpigmentation, acne vulgaris, or rosacea [24]. In 2025, scientists in Egypt compared PDT with methylene blue and IPL with IPL alone. They additionally examined treatment with only topical 10% liquid methylene blue gel. The greatest reduction in warts occurred after PDT therapy, with disappearance of 52.4%. Patients who were treated with only IPL or methylene blue gel showed poorer outcomes (19% and 4.8%) [18]. Similar results were reported in 2021, in which the cure rate after PDT sessions reached 40.9%, with clinical and dermoscopic clearance rates at 43.3%. In comparison, these rates appeared lower after IPL sessions (23.4% and 20%). In conclusion, researchers have demonstrated the superiority of PDT over IPL alone in the treatment of cutaneous warts. However, studies in which injections were involved, reported different outcomes. Both injectable treatments (Candida albicans antigen and vitamin D3) reached higher disappearance or cure rates,

with 61.5% for Candida albicans antigen and 88.89% for vitamin D3. Respectively, PDL reached 46.1% and 86.36%. While a comparison of vitamin D3 injections and PDT showed comparable outcomes, Candida albicans antigen injections demonstrated significantly better results than the PDT method [17,20].

Tolerance: Photodynamic therapy is known for being well-tolerated by patients due to its selective mechanism of action, pain-free protocols, and the simplicity of its application [16]. Although generally well-tolerated, PDT therapy can still be associated with adverse effects. The main recurrent side effect of the treatment is pain [17,19,22,23,25]. In Egyptian studies, pain outcomes varied across reports: in one study, out of 13 patients 5 experienced pain [17]; in another the VAS was 1.98 ± 1.06 in the daylight treatment group and 3.16 ± 1.05 in the pro-yellow laser group [22]; and in a thirs study, the mean pain score was 6.03 ± 2.16 [19]. Italian researchers [21] reported that their patients experienced mild burning sensation, while another study [25] reported VAS scores of 2.73 ± 1.50 after red light therapy, and 2.46 ± 1.35 after daylight. In a Chinese study conducted in 2023 apart from pain, all patients reported side effects like: mild to moderate facial erythema, swelling and epidermal peeling within the first week of treatment. Four of them developed pigmentation which mostly faded after two-three months. Minimal erythema was also reported by [22] - interestingly, patients treated with pro-yellow laser reported significantly higher occurrence of both symptoms – erythema and pain. Additionally, in a study by [25], three days following therapies, patients reported mild and moderate erythema in 39% and 23% of cases after red light therapy, and in 40% and 23% of cases after daylight therapy. Apart from side effects, a very important aspect of the therapy is its minimally destructive nature, as demonstrated in the study [21] in which lesions appeared on a tattoo that remained unchanged during and after the treatment.

Parameters: There are various types of PDT protocols that can be provided for patients. They may differ in applied photosensitizers, sources of light and its wavelength, irradiation time or even the distance from the lamp and its tilt angle.

Photosensitizers: The most commonly used photosensitizer was methylene blue (with absorption peaks at 610 and 640 nm [17]) [17–19,22]. In most of these studies, the 10% solution was used [17,18,22]. However, scientists Hassan SNE. et al. [19] injected 4% solution intralesionally. It was provided in the treatment of various types of warts, including verrucae plana [17], verrucae vulgaris [22], as well as verrucae plana, verrucae vulgaris, and verrucae plantaris [18]. 10% aminolevulinic acid was the second most common substance used by [21,23,25]. Scientists suggested this treatment to the patients with verrucae vulgaris on hands [25], verrucae plana on face [23] and on a tatoo [21]. The only study that applied a synthetic xanthene dye (Eosin Y) was [20], and it was used to treat verrucae plantaris.

Occlusion duration: In some studies, scientists specified the occlusion time, during which patients waited for illumination with the lesions covered [21,23,25]. In others patients' lesions were not covered while they were waiting for irradiation [17,20,22]. Interestingly, a delay was also applied after injection of photosensitizer [19] and it amounted to 15 minutes. The longest occlusion time was identical, at 3 hours; however, time of delay slightly differs according to the studies. The longest duration was 60 minutes [17], while in other articles it was 30 minutes [20,22].

Irradiation source: A crucial parameter of photodynamic therapy is the light source. Researchers worked with intense pulsed light with different wavelengths, the pro-yellow laser, red light, and daylight. Intense pulsed light was used in three studies with various wavelengths: 650 nm with cut-off filter [18], 640 nm with cut-off filter [17], and 560–1200 nm [19]. Similarly, red light was utilized in three articles: 630 nm [21,25] and 635 nm [23]. Additionally, in two studies daylight was used in comparison to the red light [25] and 577 nm pro-yellow laser [22]. What is more, the shortest wavelength was provided with 520 nm [20].

Irradiation time: The longest duration of illumination was reported in an Italian study by Li Pomi et al., in which patients were exposed to the daylight for 2 hours [25]. In comparison, in an Egyptian article, the duration of daylight irradiation was 15 minutes [22]. In the same study, patients were also treated with pro-yellow laser for 15 minutes [22]. What is more, red light was was used for 8 minutes in some studies [21,25] and for 20 minutes in another [23]. The shortest wavelength exposure was applied for 15 minutes [20].

Treatment duration: The frequency and duration of photodynamic therapy varied among the studies. The most commonly used schedule was sessions at 2-week intervals [17–20,23]. Patients were also treated

monthly [21,25] or one a week [22]. Scientists also suggested a different number of sessions, ranging from 8 [20], 4 [18,19,22] to 3 [17,21,23,25]. The longest treatment duration was 16 weeks (sessions every 2 weeks, up to 8 sessions) [20]. The shortest treatment lasted 4 weeks [22] and [23] - 4-6 weeks, while other procedures amounted to: 6 weeks [17]; 8 weeks [18,19] and 12 weeks [21,25].

Alleviation of pain: Although photodynamic therapy is well tolerated by patients, some researchers chose to incorporate various methods for alleviating potential pain in their studies. In three articles researchers suggested using different types of cold compress treatment [17,22,23]. However, one of them - [22] also provided 5% lidocaine cream for patients with laser treatment. What is more, one of the studies noted application of topical anesthesia under occlusion to minimize pain [19].

CONCLUSION

After analysis, photodynamic therapy showed high potential efficacy in the treatment of cutaneous warts. Comparative analyses demonstrated that PDT could be a superior form of therapy compared with intense pulsed light or topical methylene blue used alone. However, certain injection therapies, such as Candida albicans antigen or vitamin D3, may achieve comparable or even higher efficacy. PDT is generally well tolerated due to its selective mechanism of action, minimal invasiveness, and relatively simple application. Adverse effects are mostly mild and transient, including pain, erythema, swelling, and epidermal peeling, which can be alleviated using cold compresses, topical anesthetics, or lidocaine cream. What is important, PDT preserves surrounding tissue integrity, as demonstrated in studies involving lesions on tattoos. Treatment protocols vary considerably in terms of photosensitizers, light sources, wavelength, irradiation time, occlusion duration, and overall treatment schedules. Methylene blue (10%) and aminolevulinic acid are the most frequently used photosensitizers, while light sources include IPL, red light, pro-yellow laser, and daylight. Illumination duration ranges from 8 minutes to 2 hours, and treatment schedules vary from weekly to monthly sessions, with total 3 to 8 sessions. To summarize, PDT represents an effective, safe, and versatile treatment option for cutaneous warts. Optimization of parameters—including photosensitizer choice, light source, and treatment frequency—alongside supportive pain management strategies, can enhance therapeutic outcomes and patient comfort.

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